

Unconventional Interventions for PTSD: Assessing the Evidence

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This presentation describes the experimental use of devices and medications that have only been approved by the U.S. Food and Drug Administration except for research purposes

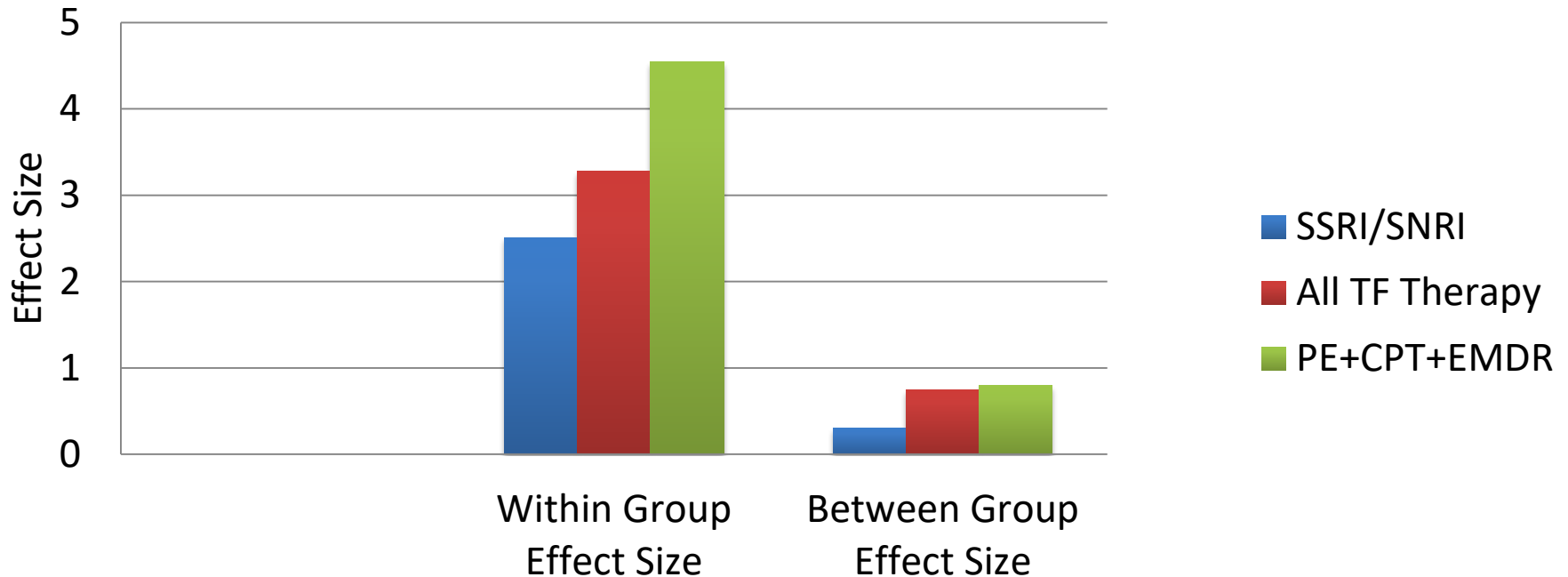
Objectives

- Describe various non-pharmacologic biological treatments proposed for PTSD
- Understand the regulatory processes applicable to various nonpharmacologic biological intervention
- Discuss the data supporting various nonpharmacologic biological interventions as potential treatments for PTSD

Overview

- Highlight the value of current evidence-based treatments for PTSD
 - And, why they might not be used
- Review the regulatory process for non-pharmacologic biological interventions
- Evaluate the data supporting the most common non-pharmacologic biological interventions:
 - Cranial Electrotherapy Stimulation (CES)
 - Magnetic Resonance Therapy (MeRT)
 - Hyperbaric Oxygen Therapy (HBOT)
 - Stellate Ganglion Block (SGB)
 - Neurofeedback

Evidence-based treatments work



PTSD Response Rates

PE/CPT/EMDR: 53%

SSRI/SNRI: 42%

No treatment: 9%

VA/DOD Clinical Practice Guideline

<https://www.healthquality.va.gov/guidelines/MH/ptsd/>

Reasons why patient/provider might not choose an EBP for PTSD

- Inaccessible
- Ineffective or residual symptoms
- Prior negative experience (patient or other)
- Comorbidity (e.g., pain)

Regulatory Process

- U.S. Food and Drug Administration
 - Approves what a company can say about its product
 - Often (but not always) assists in company getting reimbursement approval
 - Does *not* say how health care should be practiced
- Premarket approval (PMA) versus 510(K)
 - FDA-approved vs. FDA-cleared



Evaluating the Data: Concerns

- Lack of a control group
- Lack of randomization
- Placebo effects
- Sample size/publication bias
- Use of appropriate scales
 - E.g., CAPS vs. PCL vs. CGI/PGI
- Comparing effects across studies
- Acute vs. long-term effects



Dr. Margaret Patterson with an early CES system

'The Black Box' (MECANET Model IV) as shown on the RBC film, with Meg demonstrating the controls. 1980



Meg with Pete Townshend, after his treatment. 1982

Cranial Electrotherapy
Stimulation



All FDA-cleared

Cranial Electrotherapy Stimulation: Common Features

- Two or more cutaneous electrodes
 - Similar to TENS, but not TENS
- Parameters:
 - Alternating current (not TMS)
 - 0.5 to >60 Hz; up to 4 mA
 - ~30 min stimulation per day
 - Can be used over several days
- Mechanism:
 - Does not depolarize neurons
 - May alter cortical excitability of underlying cortex
 - May alter concentrations of various neurotransmitters

Efficacy

- Anxiety
 - Anecdotal, open-label data suggest effect
 - Meta-analysis of few controlled trials suggests anxiolytic effect (Klawansky et al., J Nerv Ment Dis, 1995)
 - Cochrane review: no studies qualified for inclusion
- Depression
 - Open-label studies suggest effect, but not all positive
 - RCTs mostly negative
 - Recent RCT in bipolar II depression (McClure et al, J Nerv Ment Dis 2015):
 - Positive (BDI) but very small effect size

Efficacy

- Insomnia (Electrosleep)
 - Most data anecdotal; older studies not well-designed
 - Open-label data modest
 - Controlled data generally negative but with trend toward efficacy
- Pain
 - Mixed data, with some encouraging results for:
 - Chronic pain syndromes
 - Fibromyalgia
 - Headaches/migraines
 - No definitive, randomized, controlled trials

Safety

- Noninvasive and generally well tolerated
- Potential adverse effects:
 - Irritation at site of electrodes
 - Headaches
 - Vertigo
 - Blurred vision
- No major risks or side effects

CES: Data Summary

- Published literature going back to 1960s:
 - Relatively few randomized, controlled trials
 - Generally small sample size
 - Treatment parameters heterogeneous across studies
 - Typical focus on improving symptoms vs. disorder:
 - Heterogeneous patient population (comorbidities)
 - Most studies didn't use standard outcome measures
 - Results mixed, but majority of studies report positive findings

CES: Data Summary

- FDA review (2011): “the data do not support a reasonable assurance of safety and effectiveness”
- QUERI report (2018): “the evidence is insufficient to support conclusions that CES has clinically important effects on headache, fibromyalgia, neuromuscular pain, depression, PTSD, or insomnia”

Magnetic Resonance Therapy (MeRT)



MeRT

- Essentially, transcranial magnetic stimulation
- Innovation: using EEG/EKG to guide treatment delivery
- Efficacy: no published data
- Safety: same as TMS
- Questions:
 - TMS for PTSD?
 - MeRT vs. standard TMS?

Hyperbaric Oxygen Therapy (HBOT)



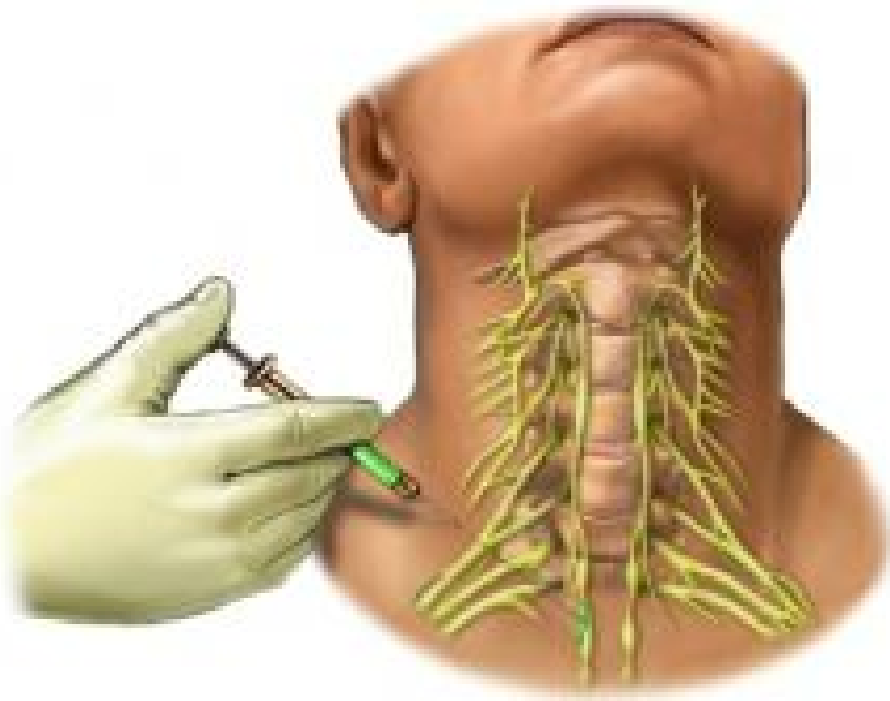
Hyperbaric Oxygen Therapy (HBOT)

- FDA-cleared for decompression sickness, carbon monoxide poisoning and several other medical conditions
- Not FDA-cleared for any psychiatric condition
- Efficacy: Three negative RCTs
- A fourth RCT showed acute benefits for post-concussive symptoms and PTSD after 13 weeks
 - BUT, positive PTSD effects were no different from sham at 6 months
 - No benefits of HBOT vs. sham at 12 months

Hyperbaric Oxygen Therapy (HBOT)

- Generally safe and well-tolerated
- Common, mild side effects:
 - Sinus pain, ear pressure, joint pain
- Rare, serious side effects:
 - Air embolism, paralysis

Stellate Ganglion Block (SGB)



- Local anesthetic injected into neck
- Target: stellate ganglion of sympathetic nervous system
- Efficacy for Complex Regional Pain Syndrome (aka Reflex Sympathetic Dystrophy)

SGB for PTSD

- Proposed mechanism: modulating the sympathetic nervous system might alter its role in PTSD in a beneficial way
- Efficacy:
 - Case series (N=9): 5 of 9 patients showed >30% improvement following 2 injections
 - Case series (N=166): ~70% showed improvement in PCL
 - RCT (N=41): no benefit of SGB vs. sham
 - Upcoming RCT (N=127): study completed Jun 2018; no results published or posted

SGB for PTSD

- Generally safe, well-tolerated
- Common side effects: neck pain, stiffness, Horner's syndrome
- Rare side effect: pneumothorax
- *Not* regulated by the FDA

Neurofeedback



Neurofeedback (NF)

- A form of biofeedback where patients are trained to modulate brain activity via real-time feedback of EEG or fMRI
- Efficacy:
 - Several studies validating proof of principle
 - RCT (N=52): EEG-based NF showed statistically significant improvements in PTSD vs. waitlist
- Safety: no concerns

Summary

- Evidence-based treatments are strongly recommended for PTSD (VA/DoD CPG)
- For patients not receiving EBPs, nonpharmacologic biological interventions might be considered
- However, data on CES, MeRT, HBOT, SGB, NF are quite limited
 - At this time, these treatments are not recommended for the treatment of PTSD